Research Article

Development of an evidence-based symptom checklist for symptoms of recurrence in women with endometrial cancer

Audra de Witt [1,2], Monika Janda[2*], Andreas Obermair[3]

[1] Menzies School of Health Research, Epidemiology and Health Systems, Spring Hill, Brisbane, Queensland, Australia, 4000.
[2] Queensland University of Technology, School of Public Health, Institute of Health and Biomedical Innovation, Brisbane, Queensland, Australia, 4059.
[3] Queensland Centre for Gynaecological Cancer, Royal Brisbane and Women's Hospital, Herston, Brisbane, Queensland, Australia, 4029.

Abstract

Objective: Women treated for endometrial cancer commonly attend clinic-based follow-up for up to five years even though there is evidence of discrepancies on effectiveness of this approach to improve survival. Furthermore, recent guidelines recommend patient education be the cornerstone for follow-up practices rather than clinical investigations such as medical imaging and tumor markers as prompt and thorough investigations of symptoms are more likely to improve survival. This current practice is based on little evidence and thus alternative models need to be investigated. The overall aim of the study is to identify currently available symptom checklists, determine the comprehensiveness of identified checklists, and generate an updated list of symptoms potentially associated with a recurrence for future testing that will lead to early recurrence detection ultimately improving survival. This paper also explores the definition of recurrence, determines recurrence rates, and identifies post treatment surveillance schedules in reviewed studies.

Methods/materials: We conducted a systematic review of the literature extracting; routine follow-up schedules; proportion of patients with symptomatic or asymptomatic recurrence; symptoms of recurrence; prevalence of these symptoms at recurrence.

Results: Overall, three previous checklists, and 12 retrospective studies were identified meeting the selection criteria. The average rate of recurrence across the studies was 13% (range 3%-19%). The proportion of patients identified with a symptomatic recurrence varied widely (overall average 67%; range 41% to 91%). The most commonly reported symptoms were vaginal bleeding (25%), pain [not further described] (16%) and abdominal pain and/or discomfort and swelling (15%) which combined, represented 56% of the total reported symptoms. The three previous checklists listed 14 and this review identified an additional 24 symptoms (e.g. vaginal discharge, extremity/bone pain and constipation) not previously identified.

Conclusion: The newly developed symptom checklist expands previous ones and will be used in a prospective study to assess sensitivity and specificity to identify recurrence compared to current standard follow-up examinations. Upon completion of successful testing in a prospective study, it could potentially provide an alternative form of follow-up to the traditional surveillance method to detect recurrences in endometrial cancer survivors.

Keywords: Endometrial cancer; symptom checklist; recurrence; follow-up care; institutional follow-up protocol.

[*]**Corresponding author**: Monika Janda, Queensland University of Technology, School of Public Health and Social Work, Institute of Health and Biomedical Innovation, Victoria Park Road, Kelvin Grove, Queensland, Australia, 4059. E-mail: m.janda@qut.edu.au
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Introduction

Endometrial cancer is the sixth most common cancer in women worldwide and is the fourteenth most common cancer overall with 320,000 new cases diagnosed in 2012 (1). A higher incidence of this cancer occurs in more developed countries with Northern America and Europe experiencing the highest incidence and Africa and Asia experiencing the lowest incidence (2) however in 2008, more than half of deaths (64%) were in developing countries (3). Survival varies widely depending on patients' age, stage at diagnosis, grade and cell type (4) and appears to be poorer in developing countries (3).

There are various types of endometrial cancer, the most common being adenocarcinomas (cancers that begin in glandular cells) (5). Other types of endometrial cancers include adenosquamous carcinoma, serous carcinoma and clear cell carcinoma, which are typically more aggressive forms of cancer (5). Tests to detect endometrial cancers typically include physical examination, transvaginal ultrasound, hysteroscopy and biopsy, computerized tomography (CT), and magnetic resonance imaging (MRI) scans (6).

Primary treatment of endometrial cancer is surgical, and includes hysterectomy and bilateral salpingo-oophorectomy, with or without surgical staging. A small number of patients are considered at high risk of local, regional or distant relapse and will be recommended postoperative radiation, chemotherapy or a combination of both. Overall 13% of patients will develop recurrence (7) with the highest risk within the first three years after primary treatment (7-9). However cancer survival is lower in less developed countries due to a range of factors including lack of access to treatment (10), lack of resources (11) and economic disadvantage (12).

The majority of patients who develop recurrences present with symptoms (51%-100%) (9, 13-19) and only a minority are diagnosed during routine follow-up visits (17-21). Furthermore, there are reports of routine follow-up leading to a delay in diagnosing recurrence as some patients wait until their next clinic visit to report symptoms (14, 18, 19, 22). Current follow-up regimes are largely based on individual hospitals' protocols. According to some authors, this has not shown to improve survival and may be ineffective (13, 14, 16, 23-25).

Despite this lack of evidence, typically women are offered follow-up commonly consisting of physical examinations every three to four months for about two years, then extending to six monthly for the subsequent three years (13, 14, 26). Recently published guidelines suggest that patient education on symptoms, rather than investigations such as medical imaging and tumour markers should be the cornerstone for patients' follow-up, as prompt and thorough investigation of symptoms is more likely to increase the chances of early detection of disease recurrence (27, 28).

To date, three symptom checklists have been developed for endometrial cancer, two for the purpose of educating patients about symptoms of recurrence, and the other for surveillance (28-30). However, the symptoms recorded in these checklists differ, and it is unknown how comprehensive these lists are.

The overall aim of this paper was to conduct, a systematic review of relevant contemporary literature to comprehensively generate an updated list of symptoms potentially associated with a recurrence of endometrial cancer. Literature searches undertaken suggests that controversies currently exist in regard to what constitutes effective surveillance management for endometrial cancer patients (22). This review explores alternative evidence based options to detect recurrences in women with endometrial cancer that will ultimately improve survival. Based on articles included in this review, this paper also explores the definition of endometrial cancer 'recurrence', determines recurrence rates in women with endometrial cancer, provides an overview of the leading symptoms of recurrence and identifies the post treatment surveillance schedules in these studies.

Materials and methods

Literature search strategy

EBSCO host (Medline complete, CIHAHL full text, PsychINFO, Academic search elite), PubMed, Web of science and Google Scholar databases were searched. Based on information obtained from article abstracts, studies conducted on the adult population and published between 1982 and 2012 were retrieved. Key search terms used included "endometr*" "cancer or neoplasm," or "carcinoma" "recurrence", "relapse", "signs," "symptoms", "surveillance" and use of MeSH terms "Endometrial neoplasms/diagnosis, rehabilitation, surgery, mortality, therapy, epidemiology, complications, nursing, prevention and control". Reference lists of articles were searched and relevant articles retrieved. Case reports, letters, editorials and papers published in a language other than English were not considered for inclusion in this review.

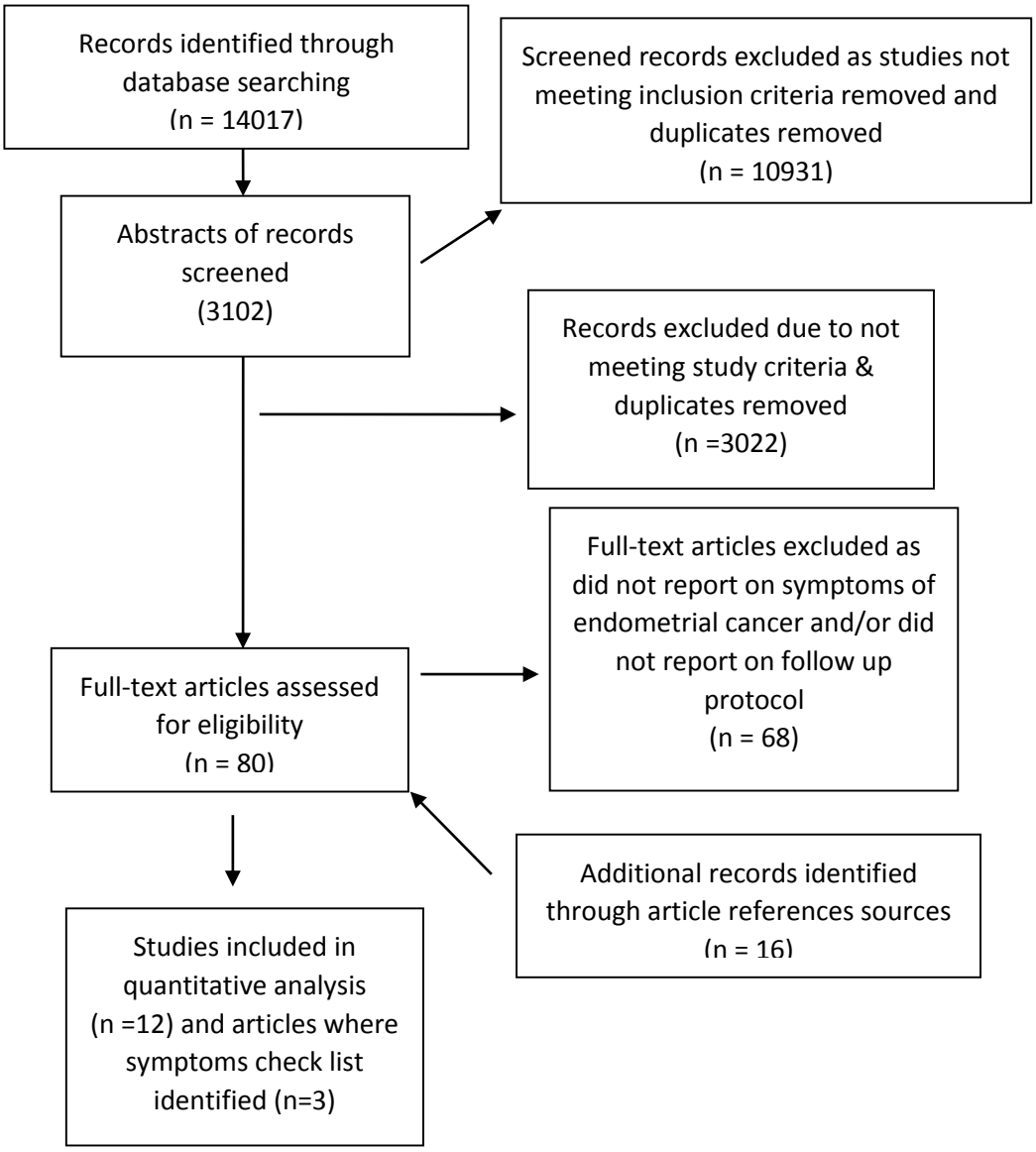

Figure 1: Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) flow diagram of article selection process

Study selection criteria and data extracted

All articles selected for inclusion in this review (Table 1) reported on original data, were from patients who received successful curative treatment for endometrial cancer, and were disease-free prior to commencing follow-up. Studies needed to provide data on; duration, year of follow-up, stage using the International Federation of Gynecology and Obstetrics (FIGO) staging systems, routine investigations undertaken, recurrence rates including the proportion of symptomatic recurrences, leading symptoms of recurrence, and time frames of scheduled follow-up protocols. We extracted data on patients' initial diagnosis (stage), the proportion of patients with symptomatic or asymptomatic recurrence, recurrence symptoms and prevalence, and routine follow-up schedules of institutions reported in studies.

Extraction of data

Data was extracted from each study. One study (26) focused on vaginal recurrences only, therefore was separated from other studies in Table 2, or excluded (Table 3) as it was not comparable to other studies which reported recurrences of all body sites. Another study was not included in Table 3 as it did not report details on symptoms of recurrences in the study population (28). In Table 3, several symptom categories from individual studies were combined into larger categories. For example, abdominal discomfort (one case), abdominal swelling (11 cases)

and abdominal pain (84 cases) were combined into a larger category of abdominal pain/discomfort/swelling (see Table 3 footnote for other combined categories).

In the event where cases may belong to more than one category, cases were counted in all relevant categories. For example, the chest/chest wall pain category (14 cases) was derived from a combination of categories reported in individual studies as follows; 'pain in chest wall' (7 cases) (19), 'cough/chest wall pain' (1 case) (14), and 'dyspnoea, dry cough, chest pain' (6 cases) (18). In the cough category, cases described above that were included in a combined category of cough and chest pain were counted in both categories under chest/chest wall pain and cough category (see Table 3 footnote).

Statistical analysis

Frequencies and proportions of recurrence presenting with or without symptoms were extracted. To estimate the proportion of patients experiencing a presenting symptom we used the formula x/y x 100 where x = the number of patients reporting the symptom and y = the total population sample that experienced recurrence symptoms. When calculating decimal points for this study, figures were rounded up if ≥ 0.5, or rounded down if ≤ 0.4 to the nearest whole number.

Results

The initial search resulted in 14,017 potentially eligible abstracts. In the first screen, abstracts of articles were reviewed against study eligibility criteria. Articles not meeting the study criteria were excluded, as were duplicate studies. The second screen involved review of full text articles by two independent assessors of which again, duplicate articles and those not meeting study criteria were removed. As a result, 12 retrospective studies were identified (Figure 1). Summary of study characteristics are presented in Table 1.

Definitions

Five of the 12 studies used a consistent definition of recurrence ('confirmed and documented disease following a minimum three month disease free interval from the time of primary treatment') (14, 18, 19, 22, 31, 32). Two studies required one month of being clinically disease free before being considered a recurrence (28), and one study defined recurrence as 'regrowth or reappearance of tumor in cases where no visible tumor was left at the completion of the operative procedure' with no time interval specified (22). Some studies did not provide an overall recurrence definition (8, 13, 17, 21) but provided local (disease limited to the pelvic cavity or vagina), and distant recurrence definitions (any disease occurring outside of the pelvis (8). In contrast, Aalders and colleagues define local recurrence as 'tumor regrowth anywhere in the pelvic structures or in the lymph nodes located below the pelvic brim' (31). In this review, where no definition was provided for disease recurrence, we assumed the definition described by Podczaski applied (22), and where no definition for local or distant recurrence was provided, we assumed the definition described by Ueda applied (8), both as described above.

The definition of symptomatic and asymptomatic disease was consistent across articles ('symptoms prior to clinical exams' and 'no complaints or symptoms but disease was detected by routine examinations' respectively) (13, 17, 21, 22, 26, 28, 31, 32). Four articles did not provide definitions, (8, 14, 18, 19) for these we assumed the definition above applied.

Recurrence rates

Of the 12 studies reviewed, three (21, 28, 32) included patients with stage 1 and stage 1-2 disease only, four studies included patients with stages 1-3, (13, 17, 19, 22) while five studies included all cancer stages (8, 14, 18, 26, 31) (Table 2).

Overall, the average rate of recurrence was 13% (range 3%-19%). The recurrence rate was lower in studies that included stage 1 (7%) and stage 1-2 (8%) cases only, compared to studies that included participants with stage 3 (16%) or stage 4 disease (14%). The proportion of patients identified with symptomatic recurrence varied widely across the studies from 41% (28) to 91% (17). On average, symptomatic recurrence rates were lower in studies that included stage 1 participants only (58%) compared to studies that included stage 1-2 (81%), stage 1-3 (68%) or all stages (67%).

Leading symptoms of recurrence

Overall, 10 of the 12 studies described in detail symptoms that led to identification of recurrence (Table 3). The most commonly reported symptoms were vaginal bleeding (25%), pain [not further described] (16%), and abdominal pain and/or discomfort and swelling (15%). Combined, these three symptoms represented 56% of the total reported symptoms in this study. In contrast, a large number of symptoms such as, fever, cardiac arrhythmia, and hemianopsia were reported in less than 1% of recurrences. Symptoms grouped into 'other' category are included in Table 3 with the contents of the

Table 1. Summary characteristics of the 12 studies reviewed

Author	Year of treatment	Duration of follow-up of participants	Routine investigations indicated by protocols
Retrospective cohort studies: FIGO Stage I & II			
Morice et al. (2001) (32)	1986-1995	Range: 12 to 137 months (Median: 42 months)	Gynaecological examination and pap smear every 3 months for the first year, 4 months during second year, 6 months during the third year and yearly thereafter. Chest X-ray and abdomino-pelviccultrasonography annually.
Salani et al. (2011) (21)	1997-2007	Range: 24 to 77 months (Mean 46 months)	Not indicated.
*Reddoch et al. (1995) (28)	1985-1992	(Median: 64 months)	Physical examination and pap smear every 3 months for the first 2 years, every 4 months for the third year, and every 6 months for the fourth and fifth years. A chest radiograph was ordered annually. Selected patients were also followed with tests of serial CA-125 levels. Computed tomographic (CT) scans were ordered based on the patients' complaints and physical findings. Many physicians also requested blood work, such as complete blood count and serum chemistries at follow-up visits.
Retrospective cohort: All cancer stages (FIGO)			
Bristow et al. (2006) (26)	1997-2005	Range: 3.4 to 143.9 months (Median: 30 months)	Pelvic examination and pap test every 3 months during the first year, 3 to 4 months during the second year and 6 monthly thereafter for total of 5 years. Chest radiograph and CT at the discretion of the treating physician, clinical risk factors and patient symptomatology.
Ueda et al. (2010) (8)	2000-2006	Range: 2 to 108 months (Median: 43 months)	Routine physical examinations, including a pelvic-rectal examination, vaginal vault cytology, and transvaginal ultrasonography (TV-USG), were performed at every visit. CT scan and chest X-ray performed biannually in the first year and annually thereafter. Tumor markers, including CA-125, one to four times annually in a subset of the cases.
Ng et al. (1997) (14)	1987-1994	Range: 3 to 90 months (Median: 43 months)	History. General examination. Cytological smear of the vault. Bimanual and recto-vaginal examination. Chest X-ray (not as routine). At every 1 to 2 months for first 2 years, every 3 months for the third year and every 6 months thereafter for 5 years.
Agboola et al. (1997) (13)	1982-1991	Range: 3 to 138 months (Median: 55 months)	Pelvic examination at each visit. Pap smear from the vaginal vault at each visit. Chest radiograph annually. Abdominal ultra sonograms, CT scans of the pelvis and abdomen and biopsies when clinically indicated.
Shumsky et al. (1994) (18)	1981-1986	Not stated	History at each visit. Cytology smears of vaginal vault at each visit. Bimanual and recto-vaginal examination at each visit. Chest X-ray biannually.

Table 1. (Continued)

Podczaski et al. (1992) (22)	1977-1987	(Median: 56 months)	Other examinations (not specified) every 3 months for 2 years, every 6 months for 3 years and yearly thereafter. Pap smear every 6 months. X-ray for first 5 years. Patients undergoing postoperative pelvic radiotherapy also underwent yearly intravenous pyelogram for 5 years after completion of treatment.
Salvesen et al. (1997) (17)	1981-1990	Range: 48 to 192 months (Median: 108 months)	Gynaecological examination and Cytological smear every 3 months for the first year, every 6 months in the second year then yearly for 8 years. Chest X-ray yearly with individually increasing intervals for 10 years with routine attendance. Ultrasound investigation were perform when clinically indicated.
Aalders et al. (1984) (31)	1960-1976	Range: 36 to 228 months	Follow-up exams every 3 months during first year. Every 6 months during second year and annually thereafter.
Case series			
Smith et al. (2007) (19)	1990-2006	(Median: 109 months)	Clinical examinations every 3 months for 2 years. Vaginal vault smears performed twice a year for first 2 years. Clinical review is then extended to once every 6 months until 5 years with vaginal vault cytology being performed once a year during this period. Additional investigations used intermittently within the follow-up period included CT scans and serum CA-125 as clinically indicated.

category varying between authors as noted in the footnote.

Symptoms checklist

Based on the reported symptoms of recurrences from these 12 studies listed in Table 3, a checklist was derived. This was compared to the three currently published symptom checklists (27, 28, 30). Table 4 demonstrates this review found 14 symptoms that are common to all three checklists and additional 24 symptoms of recurrence that were not previously identified. Examples of these additional symptoms include; vaginal discharge, extremity/bone pain and constipation.

Study follow up schedules reported in articles

Additionally, and in recognition of the ongoing debate on effectiveness of follow-up schedules, we also reviewed the reported post-treatment surveillance schedules of studies in this review which varied in the provision of details (Table 5).

In the first year, 75% of treatment centers provided one to three monthly surveillance. In the second year, 33% offered three monthly follow-ups and another 33% four monthly follow-ups (range one to six months) whereas in the third year, 50% of studies offered a six monthly follow-up schedule (three to 12 months).

Discussion

Compared to previously published symptom checklists, this review identified 24 additional symptoms of recurrence that were not previously included, and confirmed the 14 symptoms that were common to all three checklists published earlier. Only five of these symptoms were identified in one or more of these symptom checklists. Some of these additional symptoms found in this paper occurred in small numbers when studies reviewed in this paper were combined; these symptoms include fever, cardiac arrhythmia and urethral lesion. Symptoms common to all checklists include; vaginal bleeding, abdominal pain/discomfort/swelling and cough, which were identified within the top four most commonly reported symptoms in this review. Pain [not further described] was the second most common symptom in this review. Although the three previous symptom checklists included back, hip and abdominal pain, it did not include neck, leg, bone, shoulder and chest

pain, which are examples of additional symptoms identified in this review. Some symptoms were reported in one of the three checklists only; such as neuropathy, lethargy, (30) dizziness and skin lesions (28). These variations in reported symptoms may be due to reasons, such as patients' recall ability, health professionals' acuity (prompting for symptoms), health service (time constraints at appointment), and/or clinical notes recording systems (automated drop down menus restricting options).

These findings are significant as previous studies have consistently demonstrated that the majority of endometrial cancer recurrences are symptomatic (7, 9, 13-17, 19, 21, 25, 26, 28, 31, 32). This review applied stringent inclusion criteria and carefully dissected symptom reports across studies including women with differing stage of disease, and found an overall symptomatic recurrence rate of 67% which is within the 50% to 70% range reported in other studies (7, 27).

In this study, on average, symptomatic recurrence rates were lower in studies that included stage 1 participants only (58%) compared to studies that included stage 1-2 (81%), stage 1-3 (68%) or all stages (67%). Further studies need to be conducted to determine whether women with lower grades of endometrial cancer have less symptomatic recurrences compared to those with more advanced cancers. It may also suggest that women with lower grade cancers experience recurrence symptoms but these may not have significant impact on their life/lifestyle. For example, little/intermittent pain experienced and/or minor/ intermittent vaginal bleeding compared to symptomatic recurrences that occur in women with more advanced cancers, who may experience more severe pain and/or heavy vaginal bleeding. This may result in women with lower grade cancer under-reporting recurrence symptoms. However, as stated above, further investigation is required prior to reaching clear conclusions.

Table 2. Endometrial cancer recurrence rates in the identified studies

Sample/FIGO	**Total recurrences/sample**	**(%)**	**Recurrence identified by symptoms**	**(%)**
Stage 1 only				
Salani et al. (21)	4/154	(3)	3/4	(75)
Reddoch et al. (28)	39/398	(10)	14/39	(41)
Average		*(7)*		*(58)*
Stage 1 and 2 only				
Morice et al. (32)	27/351	(8)	22/27	(81)
Stage 1-3 only				
Agboola et al. (13)	50/432	(12)	30/50	(60)
^Smith et al. (19)	438/2637	(17)	199/280^	(71)
Salvesen et al. (17)	47/249	(19)	43/47	(91)
Podczaski et al. (22)	47/300	(16)	23/47	(49)
Average		*(16)*		*(68)*
Stage 1-4 (all)				
Aalders et al. (31)	379/3393	(11)	258/379	(68)
Ueda et al. (8)	29/271	(11)	13/29	(45)
Ng et al. (14)	14/86	(16)	11/14	(79)
Shumsky et al. (18)	53/317	(16)	40/53	(75)
Average		*(14)*		*(67)*
°***Overall rate*: Stage 1-4**		**(13)**		**(67)**
* Bristow et al. (26)	61/377	(16)	9/11*	(82)

^Detailed recurrence data were only available to analyse 280 patients

° Not including study by Bristow

*Study reported on vaginal recurrences only

Table 3. Symptoms of recurrence

Symptoms tally of 10 studies reviewed[1]*		
Reported symptoms	**No of occurrences (combined)**	**Total occurrences/total symptomatic reoccurrences of studies combined (%) (n=642)**
Vaginal bleeding˜	158	25
Pain	105	16
Abdominal pain/discomfort/swelling˘	96	15
Cough˙	46	7
Hemoptysis (cough blood)	35	6
Dyspnoea	32	5
Self detected/palpable mass¨	30	5
Lethargy/weight loss°	24	4
Lumbar/back pains	21	3
Urinary frequency	18	3
Pelvic pain	16	3
Pedal edema	16	3
Constipation	15	2
Chest/chest wall pain	14	2
Nausea	12	2
Gastrointestinal pain, ascites	12	2
Vaginal lesion	11	2
Vomiting	11	2
Pneumonia	11	1
Leg swelling	10	1
Diarrhea	9	1
Vaginal discharge	9	<1
DVT	8	<1
Extremity/bone pain¥	5	<1
Bowel/intestinal obstruction	4	<1
Headaches	4	<1
RUQ pain	3	<1
Pain, malignant pericardial effusion omentum	2	<1
Fever	1	<1
Cardiac arrhythmia	1	<1
Hemianopsia	1	<1
Urethral lesion	1	<1
Enlarged supraclavicular lymph node	1	<1
Crural pains	1	<1
Other#	76	12
Other^	54	8

[1] Some patients reported more than one symptom therefore total% exceeds 100%

*Reddoch study (28) did not provide symptoms detail thus was excluded from this table

* Bristow study (26) only reported on vaginal recurrences thus was excluded from this table

˜ includes two cases reported as vaginal bleeding/discharge, and nine reported cases of vaginal discharge

˘ once case abdominal discomfort, 11 cases abdominal swelling and 84 cases abdominal pain

˙includes 11 cases of cough, dyspnoea, pain, pneumonia, one case of cough/chest pain, six cases of dyspnoea, dry cough and chest pain

°lethargy and weight loss categories combined

¨categories self detected mass, palpable mass and pelvic mass combined

ˈcategories pain in chest wall, cough/chest wall pain, dyspnoea, dry cough, chest pain combined;

¥ includes one case of leg pain

Aalders study (31): edema, intestinal obstruction, anorexia, bone fracture, icterus and neurological symptoms

^ Smith study (19): fall, haematuria, hemiparesis, pain neck, discharge umbilicus, pain hip, bloating, anaemia, pleural effusion, respiratory infection, bone pain, malena, mobility problems and shoulder pain

Given the high symptomatic recurrence rate, educating survivors on commonly occurring symptoms that may indicate recurrence such as vaginal bleeding, pain, abdominal discomfort/swelling is crucial and could complement surveillance care. It is recommended that health professionals use their discretion in determining appropriate symptom recurrence information to provide to individual cancer survivors, and remind patients to promptly seek professional advice if any symptoms are experienced or concerns arise.

A number of earlier reviews have suggested limited or no increased survival benefit of intensive hospital-based follow-up surveillance for endometrial cancer survivors after receipt of primary treatment (7, 33). Furthermore, at least half of gynecologic oncology experts in a recent e-survey considered less intensive follow-up adequate for low-risk patients (6). Other surveillance suggestions include; tailoring follow-up care according to low and high risk groups (7, 18, 19, 25, 32, 34), limiting the follow-up surveillance time period (13, 26) given that 80% of recurrences occur within the first three years of follow-up (25), or, abandoning routine follow-up schedules altogether (25). These results may suggest a readiness to explore alternate forms of surveillance for recurrence detection. In response to this, we have compiled an updated and expanded symptom checklist tool to aid clinicians and patients in the detection of symptoms of recurrence. This tool could be utilized in a variety of ways. For example, it could be used by specialist consultants, general practitioners and registered nurses as a prompt at appointments to encourage discussion of symptom experiences, used as an educational tool checklist to increase patient awareness of common recurrence symptoms (based on discretion of health professional), and may also be used in less traditional methods to follow-up, such as over the telephone to discuss symptoms and/or to provide patient education. This symptom checklist is currently being tested for sensitivity and is used to trial a novel and less-intensive approach of surveillance that could potentially be used as an alternative to traditional surveillance method to detect recurrences as early as possible in endometrial cancer survivors.

In breast cancer survivors, alternative follow-up regimes have already been tested systematically and in clinical trials. For example, the provision of follow-up care by general practitioners rather than in-hospital specialists has been shown to be effective and acceptable to breast cancer patients (35). In a trial using telephone follow-up by specialist nurses after treatment for breast cancer, the telephone group were no more anxious as a result of foregoing clinic examinations and face-to-face consultations and reported higher levels of satisfaction than those attending traditional hospital clinics (36). The results of a systematic review of nurse-led versus conventional physician-led follow-up for cancer patients reported that patients appeared satisfied with nurse-led follow-up. Practical alternatives to conventional care included patient-initiated or telephone follow-up. While there were no statistically significant differences in survival, recurrence or psychological morbidity between the groups, further research is needed to determine suitability for gynecological cancer patients (37). In another study (n=36) which consisted of a clinical nurse specialist intervention among gynecological oncology patients, it was found that sexual functioning and quality of life were improved in the trial arm (38).

Current follow-up schedules (Table 5) commonly require survivors to attend about 14 hospital clinic visits within the first five years (39). In countries such as Australia, survivors often undertake extensive travel to the closest hospital for treatment. Survivors' expectations of follow-up include the prevention of recurrence or diagnoses of recurrence as early as possible (40), whereas physicians' mainly aim to see patients for on-going quality assurance and to diagnose complications as early as possible.

Limitations

This review relied on studies that had undertaken retrospective data collection or chart reviews, and the accuracy of data extracted from clinical records may vary (36). Other issues commonly relating to retrospective studies, such as missing data may have an unknown impact on the review. Additionally, reporting was often done in overlapping categories therefore a prospective study is needed to confirm that symptoms extracted here accurately reflect relevant symptoms. Variations of definitions of disease recurrence across the reviewed studies were also evident. Available data for detailed analysis were limited in some studies due to; a lack of details, no evidence of a disease-free period (19), reporting on vaginal recurrences only (26) and minimal information on follow-up schedules (30).

It is recommended that prospective cohort studies be conducted to determine alternative approaches of follow-up care for endometrial cancer patients. Randomized trials may be conducted to determine whether less intensive out of hospital follow up, or telephone care is equally effective compared to current standard care. The role of nurses in the provision of cancer follow-up care has been shown

Table 4: Comparison of previous symptom checklists to symptoms identified in this review

Comprehensive symptom checklist proposed	Previous symptom checklists		
	***SGO (30)**	***NCCN (27)**	**Reddoch et al. (28)**
Local			
Vaginal bleeding	✓	✓	✓
Vaginal discharge	-	-	-
Vaginal lesion	-	-	-
Urethral lesion	-	-	-
Urethral bleeding	✓	✓	✓
Frequent urination	-	-	-
Rectal bleeding/malena	✓	✓	✓
Rectal lesion	-	-	-
Pelvic pain	✓	✓	✓
Self detected/palpable pelvic mass	-	-	-
Hip pain	✓	✓	✓
Distant (extremities)			
Leg pain	-	-	-
Bone/extremity pain	-	-	-
Shoulder pain	-	-	-
Swollen leg(s)	✓	✓	✓
Fracture	-	-	-
Distant (abdomen & back)			
Abdominal pain/discomfort	✓	✓	✓
Abdominal swelling/ascites	✓	✓	✓
Abdominal mass	-	-	-
Loss/decreased appetite	-	✓	✓
Nausea	✓	✓	✓
Vomiting	✓	✓	✓
Constipation	-	-	-
Diarrhoea	-	-	-
Back pain/lumber pain	✓	✓	✓
Distant (thoracic & upper body)			
Chest/right upper quadrant pain	-	-	-
Neck pain	-	-	-
Headache	-	-	-
Enlarged clavicular lymph node	-	-	-
Cough	✓	✓	✓
Cardiac arrhythmia (irregular heartbeat)	-	-	-
Shortness of breath/dyspnoea	✓	✓	✓
Distant (systemic)			
Fever	-	-	-
Weight loss	✓	✓	✓
Lethargy/fatigue	✓	-	-
Anaemia/looking pale	-	-	-
Dizziness/blackout	-	-	✓
Hemiparesis/muscle weakness	-	-	-
Neuropathy/numbers	✓	-	-
Skin lesions	-	-	✓
Hemianopsia/blindness	-	-	-
Self detected mass	-	-	-

*SGO –Society of Gynaecologic Oncologist;

*NCCN – National Comprehensive Cancer Network

The symbols "✓" indicates symptom listed in the checklist and "-"denotes absence.

Table 5: Follow-up surveillance protocol of the 12 studies included in this review

	Post primary treatment follow up surveillance in the 12 identified studies											
Follow-up time	**Salani* (21)**	**Reddoch (28)**	**Morice (32)**	**Agboola (13)**	**Smith (19)**	**Salvesen (41)**	**Podczaski (22)**	**Aalders (31)**	**Ueda (8)**	**Bristow (26)**	**Ng (14)**	**Shumsky (18)**
Year 1	✓											
Monthly									✓			
1-2 monthly											✓	
3 monthly		✓	✓	✓	✓	✓	✓	✓		✓		✓
3-4 monthly												
Year 2	✓											
1-2 monthly											✓	
3 monthly		✓			✓		✓					
3-4 monthly												
3-6 monthly									✓			
4 monthly			✓	✓								✓
6 monthly												
Year 3												
3 monthly											✓	
3-6 monthly									✓			
4 monthly		✓										
6 monthly			✓	✓	✓		✓			✓		
6 monthly thereafter												✓
Annually						✓						
Annually thereafter								✓				
Year 4												
6 monthly		✓		✓	✓		✓		✓	✓	✓	✓
Annually			✓			✓						
Year 5												
6 monthly		✓		✓	✓		✓		✓	✓	✓	✓
Annually						✓						
Annually thereafter			✓									
Year 6												✓
6 monthly					✓					✓	✓	
Annually						✓			✓			
Annually thereafter				✓			✓					
Year 7												
6 monthly					✓							
Annually						✓				✓	✓	✓
Year 8												
6 monthly											✓	
Annually						✓						
Annually thereafter					✓							
Year 9												
Annually						✓						
Year 10												
Annually						✓						

*Salani study does not provide further breakdown of follow up schedules

to be valuable, cost-effective and acceptable in other cancer populations (42) thus, further research to determine suitability for endometrial cancer patients is recommended. Exploring patients' and health professionals' perspectives of follow-up care in the primary health care setting upon hospital discharge may also be of significant value to determine suitability and acceptability of this method for cancer patients.

Conclusions

The management of endometrial cancer follow-up remains controversial (22, 43, 44). There is an urgent need for a more efficient, effective and streamlined approach for endometrial cancer surveillance. Given that the majority of endometrial cancer recurrences present through symptoms, and recently published guidelines recommended patient education on symptoms be the cornerstone for patients' follow-up for recurrence detection (27, 28), the use of a symptom checklist tool could prove to be successful as one modern alternative to follow-up care for endometrial cancer survivors upon completion of successful testing within a prospective study.

This review prepares the path to examine a novel and less-intensive approach of follow-up that could potentially replace the traditional methods, ultimately aiming to enhance survivorship outcomes, improve quality of life and reduce costs.

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